Remarks

Claims 1-9 and 24-37 are pending. Claims 10-23 have been cancelled. Claims 1 and 24 have been amended. No new matter has been added.

Rejections under 35 USC § 103

Claims 1-8, 10-17 and 19-22 are rejected under 35 USC § 103(a) as being unpatentable over Avjioglu *et al.* (U.S. Pat. No. 5,480,972) in view of Colpan *et al.* (U.S. Pat. No. 6,383,393) and in view of Haj-Ahmad (U.S. Pat. No. 6,177,278). According to the Examiner, Avjioglu *et al.* teach a method of preparing a sample substantially free of genomic DNA by forming a tissue or cell lysate from a biological sample, contacting a prefiltration column with the lysate, collecting a first effluent that is substantially free of genomic DNA, contacting a second column with the effluent, and collecting a second effluent from the second column that is essentially free of genomic DNA. Colpan *et al.* teach a pre-filtration column with a filter material comprised of at least one layer of glass. Haj-Ahmad teaches a silicon carbide column using silicon carbide with an average particle size of 4.5 microns.

Claim 1 has been amended to clarify that the tissue or cell lysate loaded onto the prefiltration column contains genomic DNA. This differs from the lysate taught by Avjioglu *et al.*, which contains total RNA, *i.e.* genomic DNA, as well as proteins, are removed. While the prefiltration column used in the claimed method contains at least one layer of glass or borosilicate fiber, the column used by Avjioglu *et al.* is an oligo-(dT) cellulose column. Moreover, the role of each column is significantly different. The column of Avjioglu *et al.* binds mRNA, which is subsequently eluted from the column. In contrast, the column of the present method specifically removes genomic DNA from a complex lysate via retention by the filter (*i.e.*, only material contained in the column flow-through is further purified on a second column).

Although Colpan *et al.* teach chromatographic columns comprising glass fiber fragments, as in Avjioglu *et al.* bound nucleic acids are eluted from the column. *(See* Colpan *et al.* at column 8, lines 14-20 and claim 1). Therefore, even if the oligo-(dT) cellulose column of Avjioglu *et al.* is modified with the glass filter material taught by Colpan *et al.*, the currently claimed method remains non-obvious over the resulting method. Specifically, the currently claimed method involves contacting a prefiltration column comprising glass or

borosilicate fibers with a lysate and collecting the effluent from the column for further purification via a second column. Neither Avjioglu *et al.* or Colpan *et al.* teach or suggest collecting the effluent from the column for further processing. Haj-Ahmad's teachings regarding a silicon carbide column do not cure this deficiency.

Applicants contend that the method of claim 1 is non-obvious over Avjioglu *et al.* in view of Colpan *et al.* and in view of Haj-Ahmad. Claims 2-8 depend, either directly or indirectly from claim 1. Claims 10-17 and 19-22 have been cancelled. Therefore, Applicants request reconsideration and withdrawal of this rejection.

Claims 1 and 9 are rejected under 35 USC § 103(a) as being unpatentable over Avjioglu *et al.* in view of Colpan *et al.* and in view of Haj-Ahmad as applied to claim 1 above, and in view of the Aldrich Catalog (Aldrich Chemical Company, Milwaukee, WI, page T289 (1998/1999)). According to the Examiner, Aldrich teaches glass fibers with a specific weight of 212 g/m^2, which is within the range recited in claim 9.

Claim 1, as amended herein, is directed to a method of preparing a sample substantially free of genomic DNA by forming a tissue or cell lysate, which includes genomic DNA, as well as, other cellular components, contacting a glass or borosilicate fiber pre-filtration column with the lysate, collecting the effluent from the column, contacting a silicon carbide whisker column with the effluent, and eluting nucleic acids bound to the silicon carbide whisker column. None of the references cited by the Examiner teach or suggest, either alone or in combination, a method involving binding and retaining genomic DNA on a glass or borosilicate fiber column, collecting the effluent that flows through, and further purifying the effluent on a silicon carbide whisker column. Aldrich's teaching of a specific weight for glass fibers does not cure this deficiency. Therefore, Applicants contend that claims 1 and 9 are non-obvious over Avjioglu *et al.* in view of Colpan *et al.* and in view of Haj-Ahmad, and in view of the Aldrich Catalog. Thus, Applicants request reconsideration and withdrawal of this rejection.

Claims 10-22 are rejected under 35 USC § 103(a) as being unpatentable over Haj-Ahmad in view of Colpan *et al.* Claims 10-22 have been cancelled. Therefore, this rejection is moot and should be withdrawn.

Claim 23 is rejected under 35 USC § 103(a) as being unpatentable over Haj-Ahmad in view of Colpan *et al.* as and further in view of Crossway *et al.* (U.S. Pat. No. 4,996,144). Claim 23 has been cancelled. Therefore, this rejection is moot and should be withdrawn.

Claims 24-36 are rejected under 35 USC § 103(a) as being unpatentable over Avjioglu *et al.* in view of Colpan *et al.*, in view of Haj-Ahmad and in view of Dove *et al.* (U.S. Patent No. 5,006,472). According to the Examiner, Avjioglu *et al.* teach a method of preparing a sample substantially free of genomic DNA by forming a tissue or cell lysate from a biological sample, contacting a prefiltration column with the lysate, collecting a first effluent from the prefiltration column that is substantially free of genomic DNA, contacting a second column with the first effluent, and collecting a second effluent from the second column, which is essentially free of genomic DNA.

As discussed above, in the claimed method of the invention, the tissue or cell lysate loaded onto the prefiltration column contains genomic DNA, which differs from the lysate taught by Avjioglu *et al.*, which contains total RNA (*i.e.* genomic DNA, as well as proteins, are removed). While the prefiltration column used in the claimed method contains at least one layer of glass or borosilicate fiber, the column used by Avjioglu *et al.* is an oligo-(dT) cellulose column. Moreover, the role of each column is significantly different. The column of Avjioglu *et al.* binds mRNA, which is subsequently eluted from the column. Although the eluted material may technically be considered a column effluent, it differs from the effluent of the claimed method, which is comprised of the unbound components of the prefiltration column flow-through. Therefore, the column of the present method specifically removes genomic DNA from a complex lysate via retention by the filter.

Although Colpan *et al.* teach chromatographic columns comprising glass fiber fragments, as in Avjioglu *et al.* bound nucleic acids are eluted from the column. *(See* Colpan *et al.* at column 8, lines 14-20 and claim 1). Therefore, even if the oligo-(dT) cellulose column of Avjioglu *et al.* is modified with the glass filter material taught by Colpan *et al.*, the currently claimed method remains non-obvious over the resulting method. Specifically, the currently claimed method involves contacting a prefiltration column comprising glass or borosilicate fibers with a lysate and collecting the effluent from the column for further purification via a second column. Neither Avjioglu *et al.* or Colpan *et al.* teach or suggest collecting an effluent containing material that does not bind to the column for further processing. Neither Haj-Ahmad's teachings regarding a silicon carbide column or Dove *et*

al.'s disclosure regarding contacting nucleic acids bound to a column with DNase cure these deficiencies. Therefore, Applicants assert that claims 24-36 are non-obvious over Avjioglu *et al.* in view of Colpan *et al.*, in view of Haj-Ahmad and in view of Dove *et al.* Thus, Applicants request reconsideration and withdrawal of this rejection.

Claim 37 is rejected under 35 USC § 103(a) as being unpatentable over Avjioglu *et al.* in view of Colpan *et al.*, in view of Haj-Ahmad, in view of Dove *et al.* as applied to claim 34 above, and further in view of Crossway *et al.* According to the Examiner, while Colpan *et al.* teach DNA digestion, neither Avjioglu *et al.*, Haj-Ahmad or Dove *et al.* teach additional digestion with DNase. However, Crossway *et al.* teach a method of purification of nucleic acids using additional digestion with DNase with the added benefit of allowing differential detection of RNA only.

Claim 1, as amended herein, is directed to a method of preparing a sample substantially free of genomic DNA by forming a tissue or cell lysate, which includes genomic DNA, as well as, other cellular components, contacting a glass or borosilicate fiber pre-filtration column with the lysate, collecting the effluent from the column, contacting a silicon carbide whisker column with the effluent, treating the silicon carbide-bound nucleic acids with DNase, eluting nucleic acids bound to the silicon carbide whisker column, and adding DNase to the eluate. None of the references cited by the Examiner teach or suggest, either alone or in combination, a method involving binding and retaining genomic DNA on a glass or borosilicate fiber column, collecting the effluent that flows through, and further purifying the effluent on a silicon carbide whisker column. Crossway *et al.*'s teaching of DNase digestion does not cure this deficiency. Therefore, Applicants contend that claim 37 is non-obvious over Avjioglu *et al.* in view of Colpan *et al.* and in view of Haj-Ahmad, in view of Dove *et al.*, and further in view of Crossway *et al.* Thus, Applicants request reconsideration and withdrawal of this rejection.

Nonstatutory Double Patenting

Claims 1 and 7-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 and 14 of copending Application No. 10/914,920 in view of Haj-Ahmad. According to the Examiner, both sets of claims are drawn to methods of purification using pre-filtration columns having a

glass or borosilicate layer and contacting the effluent with a second column that allows separation of RNA. Claims 1, 7-12 and 14 of the '920 application are silent with respect to silicon carbide whiskers, however Haj-Ahmad teaches purification of RNA using silicon carbide particles. The Examiner concludes that it would have been obvious to modify the claims of the '920 application with the silicon carbide particles as taught by Haj-Ahmad with a reasonable expectation of success, and the ordinary artisan would have been so motivated because the modification would have resulted in use of an economically efficient medium for use in purification of nucleic acids. Applicants traverse.

Applicants submit herewith a terminal disclaimer in compliance with 37 CFR 1.321(c) along with the appropriate fee under 37 CFR 1.29(d). Copending Application No. 10/914,920 and the instant application are commonly owned by Agilent Technologies Inc. Therefore, Applicants request reconsideration and withdrawal of this rejection.

In accordance with Section 714.01 of the M.P.E.P., the following information is presented in the event that a call may be deemed desirable by the Examiner:

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Respectfully submitted,

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